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PATENT
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Washington, D.C. 20231

By: Maisie C. Livengood
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Empedocles, et al.

Application No.: 09/784,645

Filed: February 15, 2001

For: MICROARRAY METHODS UTILIZING SEMICONDUCTOR NANOCRYSTALS

Examiner: Forman, Betty J.

Art Unit: 1634

AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed May 9, 2002, please amend the above-identified application as shown below. The deadline for response to the Office Action is August 9, 2002. A petition to extend the period for response for one month is enclosed herewith, thus extending the period of response until September 9, 2002. Accordingly, this response is timely filed.

IN THE SPECIFICATION:

Please replace the paragraph beginning at page 60, line 34 with the following rewritten paragraph:

B1

Semiconductor nanocrystals can be utilized to label various target biomolecules for use in various types of secondary interrogations. Such investigations generally involve

conducting an additional analysis once a binding complex between two or more biomolecules have already been formed. The array in such investigations typically bears a biomolecule that captures a target molecule in preparation for a secondary interrogation. Suitable targets in this type of study include, but are not limited to, nucleic acids (*e.g.*, DNA, RNA), proteins, or antibodies.

IN THE CLAIMS:

Appendix A entitled "Version with Markings to Show Changes Made" is attached hereto and shows the amendments to the following claims. Appendix B entitled "Pending Claims" which is attached hereto provides a clean version of all the claims as pending following entry of this amendment.

Please cancel claims 11, 12, 14, 15, 25 and 26 and amend the following claims as indicated without prejudice or disclaimer.

1. (Once amended) An analytical method of detecting a ligand of interest in a sample, comprising:

(a) providing a first plurality of antiligands immobilized on a solid support at positionally distinct locations thereon to provide a first array, wherein the plurality of antiligands comprises a first antiligand capable of binding specifically to a first ligand of interest;

(b) contacting the array with a sample containing or suspected of containing the first ligand, wherein the first ligand is linked through a linker to a first semiconductor nanocrystal before, during or after the contacting, under conditions in which the first ligand, if present, binds specifically to the first antiligand to form a first complex;

(c) optionally, removing unbound ligand from the array; and

(d) identifying the location of the first complex by detecting and, optionally, quantifying the presence in the first complex of the first semiconductor nanocrystal, detection of the first semiconductor nanocrystal indicating the presence of the first ligand of interest.

B3

3. (Once amended) The method of claim 1, wherein

the sample contains a second ligand linked to a second semiconductor nanocrystal which is detectably distinct from the first semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized antiligand to form a second complex; and

identifying comprises determining which location or locations of the array include the first complex, the second complex or the first and second complexes by detecting and, optionally, quantifying simultaneously or sequentially the presence in the first and second complexes of the first and second semiconductor nanocrystals.

B4

8. (Once amended) The method of claim 6, wherein the first ligand is linked to a single first semiconductor nanocrystal.

9. (Once amended) The method of claim 7, wherein the first ligand and the second ligand are linked to a single first and a single second semiconductor nanocrystal, respectively.

B5

19. (Once amended) The method of claim 16, wherein

the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal that is capable of binding specifically to a second immobilized antiligand to form a second complex; and

identifying comprises determining which location or locations of the array include the first complex, the second complex or the first and second complexes by detecting and, optionally, quantifying simultaneously or sequentially the presence in the first and second complexes of the first and second semiconductor nanocrystals.

B6

21. (Once amended) The method of claim 20, wherein

the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal that is capable of binding specifically to a second immobilized antiligand to form a second complex; and

B4 cnt.

identifying comprises determining which location or locations of the array include the first complex, the second complex or the first and second complexes by detecting and, optionally, quantifying simultaneously or sequentially the presence in the first and second complexes of the first and second semiconductor nanocrystals.

B7

40. (Once amended) An analytical method, comprising:

(a) providing a first plurality of antiligands immobilized on a solid support at positionally distinct locations thereon to provide an array, wherein the plurality comprises a first antiligand that is a binding partner of a first ligand;

(b) contacting the first array with a sample containing or suspected of containing the first ligand, whereby the first ligand, if present, and the first antiligand interact to form a first complex;

(c) labeling the first ligand in the first complex with a first semiconductor nanocrystal; and

(d) identifying which location of the array includes the first complex by detecting the presence therein of the first semiconductor nanocrystal, detection of the first semiconductor nanocrystal indicating the presence of the first ligand.

41. (Once amended) The method of claim 40, wherein:

the first plurality of antiligands comprises a second antiligand that is a binding partner of a second ligand;

the sample contains or is suspected of containing the second ligand, whereby the second ligand and the second antiligand interact to form a second complex;

step (c) comprises labeling the second ligand in the second complex with a second semiconductor nanocrystal that is detectably distinct from the first semiconductor nanocrystal; and

step (d) comprises determining which location or locations of the array include the first complex, the second complex or both the first and second complexes by detecting the presence therein of the first and second semiconductor nanocrystals.

B7 Cont.

42. (Once amended) The method of claim 40, wherein the first ligand comprises a first member of a first binding pair and the semiconductor nanocrystal is linked to a second member of the first binding pair through a linker.

REMARKS

I. Status of the Claims

Claims 1-43 are currently pending in this application, with claims 27-39 withdrawn as being directed to a non-elected invention. Upon entry of this amendment, claims 11, 12, 14, 15, 25 and 26 are canceled and claims 1, 3, 8, 9, 19, 21, 40, 41 amended without prejudice or disclaimer.

II. Claim Objections

Claim 25 has been canceled, thus rendering moot the objection to this claim; claims 40 and 42 have been amended as recommended by the Examiner.

III. Claim Rejections under 35 U.S.C. §112

Claims 1-26, 41 and 43 stand rejected as allegedly being indefinite. The claims have been amended as suggested by the Examiner. Thus, it is requested that this ground of rejection be withdrawn.

IV. Claim Rejections under 35 U.S.C. §102

Claims 1-10, 13, 16-24 and 40-43 stand rejected under U.S.C. §102(e) as allegedly being anticipated by U.S. Patent No. 6,306,610 to Bawendi et al. ("Bawendi"). For the reasons that follow, Applicants respectfully disagree.

A. Currently Claimed Invention

The claims that are alleged to be anticipated by Bawendi are all directly or indirectly dependent upon claims 1 or 40. The method as recited in claim 1 involves providing an array in which a plurality of antiligands are immobilized on a solid support at positionally

distinct locations. This array is contacted with a sample that contains, or is suspected of containing, a ligand that is linked through a linker to a semiconductor nanocrystal. The array and sample are contacted under conditions such that the ligand, if present in the sample, binds to an antiligand on the array to form a complex. Linking of the ligand and semiconductor nanocrystal can occur before or after the array and sample have been brought into contact. Unbound ligands can optionally be removed from the array. The location of the complex on the array is then identified by detecting the presence in the complex of the semiconductor nanocrystal. The amount of semiconductor nanocrystal at the location can optionally be quantified.

Claim 40 also describes an array-based method for analyzing interactions between a ligand and antiligand on an array. In this particular method, the ligand that binds an antiligand on the array is not labeled with a semiconductor nanocrystal until *after* the ligand and antiligand have interacted to form a complex. This approach can have advantages over conventional methods in which the ligand is already labeled before it is contacted with the array in that the semiconductor nanocrystal is not present to interfere with the interaction between the ligand and antiligand as they form a complex (see, e.g., page 32, line 11-17).

B. Bawendi Distinguished

The Office Action at page 4 contends that a specific section in Bawendi (col. 22, lines 48-65 and Figure 2) anticipates the foregoing claims. The section that is cited, however, merely describes a solid phase immunoassay. This section, as well as the rest of Bawendi, fails to teach or suggest several elements of the currently claimed invention as required for an anticipation rejection.

For example, Bawendi does not teach or suggest an array in which a ligand is immobilized at "positionally distinct locations" on a solid support as specifically recited in both claims 1 and 40. Instead, Bawendi simply discusses attachment of an antibody to a solid phase in general terms. Additionally, Bawendi does not teach or suggest identifying the location on the array of a complex by detecting the presence in the complex of a semiconductor nanocrystal as required in both claims 1 and 40.

Claim 40 and its dependent claims are further distinguished from Bawendi in that, as claimed, labeling of ligand with a semiconductor nanocrystal does not occur until *after* the ligand has interacted with an antiligand on the array to form a complex. As noted above, this can be useful in preventing the semiconductor nanocrystal from interfering with the formation of a complex between a ligand and an antiligand. Bawendi does not teach or suggest such a method; instead, Bawendi only discusses methods in which ligands are labeled with semiconductor nanocrystals *before* the ligand is contacted with the antiligand.

For all these reasons, Bawendi fails to anticipate claims 1-10, 13, 16-24 and 40-43. Accordingly, it is respectfully submitted that this ground of rejection should be withdrawn.

V. Claim Rejections under 35 U.S.C. §103

Claims 11, 12, 25 and 26 are rejected under 35 U.S.C. §103(a) as obvious over Bawendi in view of PCT publication WO 99/31275 to Gold et al. ("Gold"). Claims 14 and 15 are rejected under 35 U.S.C. §103(a) as obvious over Bawendi and U.S. Patent No. 5, 605, 798 to Koster et al. ("Koster").

While not agreeing with these conclusions, these claims have been canceled without prejudice or disclaimer to advance prosecution of important subject matter, thereby rendering this ground of rejection moot.

It is submitted that the other pending claims are not obvious over these cited references because, even when combined, the references fail to teach or suggest each and every element of the claims. More specifically, as described supra, Bawendi fails to teach several elements of claims 1 and 40; the other cited references do not compensate for these deficiencies in Bawendi.

VI. Double Patenting Rejections

Claims 1-10, 16-26 and 40-43 are rejected under obviousness-type double patenting over claims 1-40 of U.S. Patent No. 6,274,323 in view of U.S. Patent No. 5,606,789 to

Koster. Applicants will submit a terminal disclaimer to overcome this rejection upon notification of allowable subject matter.

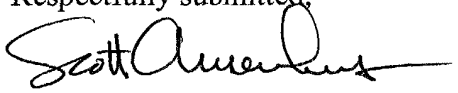
Claims 1-10, 16-26 and 40-43 are provisionally rejected under obviousness-type double patenting over claims 1-6 and 12-15 of copending application 09/784,866. Claims 1-10, 20-26 and 40-43 are provisionally rejected under obviousness-type double patenting over claims 1-11, 17-22 and 28-39 of copending application 09/766,273 and over claims 1-18 of copending application no. 09/882,193. Because these are provisional double patenting rejections, Applicants request that this rejection be held in abeyance pending notification of allowable subject matter.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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